

Lenn

June 8, 1959

London

Dear Joe:

Esther and I are now on the last leg of our trip and should be home just about the time you get this. All the best luck to you in your new laboratories!

The symposia we've attended have been quite instructive, especially the one at Royaumont on cellular immunity of which I am enclosing the abstracts. It is hard to escape the feeling, which I know you already share, that immunology is in for a new era of importance in medicine, and with this a new challenge to the pharmaceutical industry. I would urge you to be especially attentive to this field to be ready to exploit its developments at the earliest moment. The most important step, not yet quite achieved, may be the artificial cultivation of functionally active 'immunocytes'-- cells of the lymphoid system involved in antibody production.

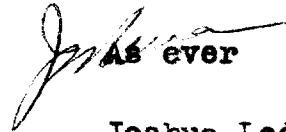
The lines of development I can foresee include:

1. Agents which interfere with the primary immune response, as well as with its terminal effects. We have already discussed screening for such agents from microbial broths; there would also be the further possibility of 'substitutional chemotherapeutic' methods. To the systems for screening for the terminal effects we have also already discussed, I might add now the inhibition of antibody cytotoxicity (cf. Gorer) on leukemia cells, which may or may not be equivalent to complement fixation and immune lysis of RBC. Miescher's system of the inhibition of clot retraction through the effect of Ag-Ab complexes on platelets may also be quite promising as an in vitro method.

2. Production of specific antibodies through in vitro culture of clones of (human?) immunocytes. This still needs some important advances in technique.

3. A revival of serotherapy in which the antibody-specific fragment of antibody is isolated to avoid the antigenicity of the globulin carrier. This is based on the work of Porter and others (Nature 1958-- full reference in my article on genes and antibodies) on the splitting by papain of rabbit XX Ab globulins into a common antigenic fragment and a differential fragment, not antigenic, having the specific combining ability of the Ab. It is not yet known whether the Ab-fragment has any protective value in infection: if it does it may be the basis of a revival of serum therapy, and I strongly recommend you look into this.

As a temporary expedient, someone ought to inquire whether serum sickness, brought about by sensitization to, say, rabbit antibody globulin, could be mitigated by the injection of anti-globulin antibodies from other species. A human anti-rabbitglobulin serum might be the ideal reagent, but expensive. The argument would be that an excess of circulating antibody should facilitate the clearance of the offending antigen, the persistence of which is a troublesome feature in serum sickness. I haven't ~~xxxx~~ had the chance to review any literature in this¹ field.

As ever

Joshua Lederberg

P.S. I left out one of the most exciting prospects -- See Lawrence's abstract (and a symposium he edited, 1959, Hypersensitive States, Hoeber-Harper publ.) You might market the antibody-producing microsomes to transplant direct to recipients, as a substitute for potentially dangerous vaccines.